ABSTRACT

THESIS: Role of Apj Signaling in the Regulation of Cardiac Progenitor Stem Cells that Give Rise to Aorta and Pulmonary Trunk in Mice

STUDENT: Kamal Baral

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Apelin receptor (APJ) provides cellular instructions for cardiovascular development in mice. During embryonic mouse heart development, APJ is expressed by a small subset of cardiac progenitors found in the second heart field (SHF) region. We show that APJ+ cells contribute to the cells of outflow tract (OFT), which eventually give rise to aorta and pulmonary trunk upon its morphogenesis. The role of APJ in SHF domain is unclear. The main objective of this research is to identify the exact role of APJ in outflow tract development by analyzing its function early in cardiac progenitors in the SHF and later in the events of OFT morphogenesis. We hypothesize that APJ stimulate SHF progenitor cell growth and contribute to the morphogenesis of aorta and pulmonary trunk. To address this hypothesis, we studied the effect of SHF progenitor cell specific *Apj* gene deletion on the proliferation and survival of OFT progenitors in the SHF domain and its impact on the morphogenesis of OFT in the developing heart. Our data suggested that the deletion of *Apj* gene reduced the proliferation of SHF progenitors, while there was no significant impact of *Apj* deletion on survival of the SHF progenitors. Morphological analysis by whole mount immunostaining of intact whole heart revealed double outlet ventricle and misalignment of aorta and pulmonary trunk. Moreover, the *Apj* deletion led to OFT related

phenotypes. Our findings provide a novel role for APJ in the regulation of SHF cardiac progenitors and their contributions to aorta and pulmonary trunk formation.